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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,353	02/26/2004	Arthur M. Krieg	C1039.70083US07	9688

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Helen C. Lockhart, Ph.D.  
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600 Atlantic Avenue  
Boston, MA 02210

EXAMINER
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ARCHIE, NINA

ART UNIT	PAPER NUMBER
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1645

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11/10/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/789,353	<b>Applicant(s)</b> KRIEG ET AL.	
	<b>Examiner</b> Nina A. Archie	<b>Art Unit</b> 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 February 2010 and 06 April 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 28,29,31-33 and 36 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 28-29, 31-33, and 36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

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### **DETAILED ACTION**

#### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 1, 2010 and April 6, 2010 has been entered.

The declaration filed on 3/12/2009 by Cy Stein has been considered.

#### ***Amendment Entry***

2. The amendment filed February 1, 2010 has been entered. Claims 28-29, 31-33, and 36 have been amended. Claims 1-27, 30 and 34-35 are cancelled. Claims 28-29, 31-33, and 36 are pending and under examination.

#### ***Withdrawal of Rejection***

3. The rejection of claims 28-29, 31-33, and 36 under 35 U.S.C. 103(a) as being unpatentable over (Kuramoto et al 1992 Jpn J. Cancer Res Vol. 83 pgs. 1128-1131) in view of (Goodchild et al 1990 The American Chemical Society, Vol. 1, No. 3 pgs. 165-182), (Hutcherson et al US Patent 5,723,335 March 3, 1998 (filed March 25, 1994)), and (Cheng et al US Patent No. 5,646,126 July 8, 1997 (filed February 28, 1994)) has been withdrawn in view of applicants amendments thereto and applicants arguments.

#### ***Response to Arguments***

4. Applicant's arguments with respect to claims 28-29, 31-33, and 36 have been considered but are moot in view of the ground(s) of rejection.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 28-29, 31-33, and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The independent claims 28-29, recite the phrase "immunostimulatory oligonucleotide comprising 5' AACGTT". It is unclear whether the phrase "immunostimulatory oligonucleotide comprising 5' AACGTT" encompasses an unmethylated C, although the specification discloses an immunostimulatory oligonucleotide is required to have at least an unmethylated C to be deemed the immunostimulatory (see specification pg. 7 lines 10-20). Therefore the skilled artisan would not be readily apprised of the metes and bounds of "immunostimulatory oligonucleotide comprising 5' AACGTT" nor how to assess such. Clarification in this regard is required.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 28-29, 31-32, and 36 under 35 U.S.C. 103(a) as being unpatentable over (Hutcherson et al US Patent 5,723,335 March 3, 1998 (filed March 25, 1994)) in view of (Kuramoto et al 1992 Jpn J. Cancer Res Vol. 83 pgs. 1128-1131).

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The claims are drawn to an immunostimulatory oligonucleotide, comprising: 5'-AACGTT-3', 8-40 nucleotides in length, wherein each internucleotide linkage has a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate (claim 28), an immunostimulatory oligonucleotide, comprising: 5'-AACGTT-3', 8-40 nucleotides in length, having at least one phosphate backbone modification, wherein the oligonucleotide is linked to a nucleic acid delivery complex (claim 29); wherein the oligonucleotide is covalently linked to a nucleic acid delivery complex (claim 31), wherein the oligonucleotide is covalently linked to a nucleic acid delivery complex is a cationic lipid (claim 32), a composition comprising the immunostimulatory oligonucleotide and a pharmaceutically acceptable carrier (claim 36).

Hutcherson et al teach a composition (see column 5 lines 40-67, column 6 lines 31-43, column 7 lines 55-67, column 10 lines 46-57) comprising: an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains an immunostimulatory CpG oligonucleotide associated (covalently) with a cationic lipid, wherein the CpG includes a phosphate backbone modification is a phosphorothioate (see abstract, column 5 lines 40-59, column 8 lines 31-50). Hutcherson et al teach a composition comprising a pharmaceutically acceptable carrier (see column 7 lines 49-55), wherein the oligonucleotide is synthetic (see column 8 lines 32-41). Hutcherson et al teach oligonucleotides analogs are useful as immunopotentiators and certain antisense oligonucleotides possess anti-infective and anticancer effects which are enhanced through immune stimulation (see column 5 lines 7-10).

Hutcherson et al does not specifically teach 5'-AACGTT-3', 8-40 nucleotides in length in an immunostimulatory oligonucleotide, wherein each internucleotide linkage in the 5'-AACGTT-3' has a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate.

Kuramoto et al teach an oligonucleotide, comprising: 5'-AACGTT-3', 8-40 nucleotides in length with a modified backbone. Kuramoto et al teach AACGTT is a potent palindrome and further teach the oligonucleotides containing 5'-AACGTT-3' enhance NK cell activity (see abstract, pg. 1128 columns 1 and 2), wherein the oligonucleotide with 5'-AACGTT-3' showed the strongest NK cell activity (see pg. 1129 column 2 paragraph 2). Kuramoto et al teach strong immunostimulatory activity of certain oligonucleotides maybe due to the potent palindromes (i.e. AACGTT) (see pg. 1131 column 2). Thus oligonucleotide of Kuramoto et al necessarily has

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immunological and biological properties as that of the instant invention thus the oligonucleotide of Kuramoto et al have immunostimulatory activity as evidenced to the contrary. Therefore the immunostimulatory oligonucleotide of Kuramoto et al inherently anticipate the claimed invention in the prior art.

It would have been prima facie obvious at the time the invention was made to employ the immunostimulatory oligonucleotide comprising 5'-AACGTT-3', 8-40 nucleotides in length (as disclosed by Kuramoto et al) as an immunostimulatory oligonucleotide, with a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate, wherein each internucleotide linkage has a phosphate backbone modification (as disclosed by Hutcherson et al) in order to take advantage of using the features of oligonucleotides with at least one or additional inter-sugar linkages (i.e. phosphorothioate) such as enhancing the uptake into cells and enhancing stability and affinity of the oligonucleotide, which have been demonstrated to affect humoral and cell-mediated immune responses.

One would have a reasonable expectation of success because the use of certain antisense oligonucleotides having at least one phosphorothioate bond enhance immune stimulation (as disclosed by Hutcherson et al) is well known in the art.

Hutcherson et al demonstrates oligonucleotide immunopotentiators having at least phosphorothioate bond which are capable of eliciting an immune response are well established in the art. Kuramoto et al teach an oligonucleotide, comprising: 5'-AACGTT-3', 8-40 nucleotides in length with a modified backbone and strong immunostimulatory activity of certain oligonucleotides maybe due to the potent palindromes as being well known in the art. Thus leading to predictable results, it would be obvious to use the cited immunostimulatory oligonucleotide comprising 5'-AACGTT-3', (as disclosed by Kuramoto et al) as an immunostimulatory oligonucleotide, with a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate, wherein each internucleotide linkage has a phosphate backbone modification (as disclosed by Hutcherson et al). Thus, it remains obvious to combine them (Hutcherson et al and Kuramoto et al), in order to take advantage of using the features of oligonucleotides with at least one or additional inter-sugar linkages (i.e. phosphorothioate) such as enhancing the uptake into cells and enhancing stability and affinity of the oligonucleotide, which have been demonstrated to affect humoral and cell-mediated immune responses. KSR forcloes the argument that a specific

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teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board Decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007 (citing *KSR*, 82 USPQ2d at 1396) available at <http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>).

Hutcherson et al demonstrates oligonucleotides having at least one phosphorothioate bond are immunopotentiators with the ability to enhance uptake into cells and enhance stability and affinity of an oligonucleotide which affect humoral and cell-mediated immune responses. Kuramoto et al teach strong immunostimulatory activity of certain oligonucleotides may be due to the potent palindromes. Hutcherson et al and Kuramoto et al disclose the teachings aforementioned above and also are well known in the art. Therefore, the immunostimulatory oligonucleotide comprising: 5'-AACGTT-3' of Kuramoto et al is well within the capabilities for one of ordinary skill in the art to be obvious to modify the immunostimulatory oligonucleotide comprising 5'-AACGTT-3', 8-40 nucleotides in length (as disclosed by Kuramoto et al) wherein the backbone is modified by phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate, wherein each internucleotide linkage has a phosphate backbone modification (as disclosed by Hutcherson et al). The *KSR* decision sets forth "if a technique has been used to improve one device, and a person of skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill". Thus, the requirements of obviousness under the *KSR* decision are met.

7. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over (Hutcherson et al US Patent 5,723,335 March 3, 1998 (filed March 25, 1994)) in view of (Kuramoto et al 1992 *Jpn J. Cancer Res Vol. 83* pgs. 1128-1131) as applied to claims 28-29, 31-32 and 36 above, and further in view of (Cheng et al US Patent No. 5,646,126 July 8, 1997 (filed February 28, 1994)).

The claims are drawn to an immunostimulatory oligonucleotide, comprising: 5'-AACGTT-3', 8-40 nucleotides in length, wherein each internucleotide linkage has a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate (claim 28), an immunostimulatory oligonucleotide, comprising: 5'-AACGTT-3', 8-40 nucleotides in length, having at least one phosphate backbone modification, wherein the oligonucleotide is linked to a nucleic acid delivery complex (claim 29); wherein the oligonucleotide is covalently linked to a

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nucleic acid delivery complex (claim 31), wherein the oligonucleotide is covalently linked to a nucleic acid delivery complex is a (cationic lipid) (sterol) (claims 32-33); a composition comprising the immunostimulatory oligonucleotide and a pharmaceutically acceptable carrier (claim 36).

Hutcherson et al teach a composition (see column 5 lines 40-67, column 6 lines 31-43, column 7 lines 55-67, column 10 lines 46-57) comprising: an oligonucleotide delivery complex, wherein the oligonucleotide delivery complex contains an immunostimulatory CpG oligonucleotide associated (covalently) with a cationic lipid, wherein the CpG includes a phosphate backbone modification is a phosphorothioate (see abstract, column 5 lines 40-59, column 8 lines 31-50). Hutcherson et al teach a composition comprising a pharmaceutically acceptable carrier (see column 7 lines 49-55), wherein the oligonucleotide is synthetic (see column 8 lines 32-41). Hutcherson et al teach oligonucleotides analogs are useful as immunopotentiators and certain antisense oligonucleotides possess anti-infective and anticancer effects which are enhanced through immune stimulation (see column 5 lines 7-10).

Hutcherson et al does not specifically teach 5'-AACGTT-3', 8-40 nucleotides in length in an immunostimulatory oligonucleotide, wherein each internucleotide linkage in the 5'-AACGTT-3' has a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate. Hutcherson et al does not teach an immunostimulatory oligonucleotide, wherein the nucleic acid delivery is a sterol.

Kuramoto et al teach an oligonucleotide, comprising: 5'-AACGTT-3', 8-40 nucleotides in length with a modified backbone. Kuramoto et al teach AACGTT is a potent palindrome and further teach the oligonucleotides containing 5'-AACGTT-3' enhance NK cell activity (see abstract, pg. 1128 columns 1 and 2), wherein the oligonucleotide with 5'-AACGTT-3' showed the strongest NK cell activity (see pg. 1129 column 2 paragraph 2). Kuramoto et al teach strong immunostimulatory activity of certain oligonucleotides maybe due to the potent palindromes (i.e. AACGTT) (see pg. 1131 column 2). Thus oligonucleotide of Kuramoto et al necessarily has immunological and biological properties as that of the instant invention thus the oligonucleotide of Kuramoto et al have immunostimulatory activity as evidenced to the contrary. Therefore the immunostimulatory oligonucleotide of Kuramoto et al inherently anticipate the claimed invention in the prior art.



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Cheng et al teach an oligonucleotide modified with a phosphorothioate backbone covalently linked to a sterol which correlates to an oligonucleotide covalently linked to an nucleic delivery complex as a sterol.

It would have been prima facie obvious at the time the invention was made to employ the immunostimulatory oligonucleotide comprising 5'-AACGTT-3', 8-40 nucleotides in length (as disclosed by Kuramoto et al) as an immunostimulatory oligonucleotide, with a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate, wherein each internucleotide linkage has a phosphate backbone modification (as disclosed by Hutcherson et al) in order to take advantage of using the features of oligonucleotides with at least one or additional inter-sugar linkages (i.e. phosphorothioate) such as enhancing the uptake into cells and enhancing stability and affinity of the oligonucleotide, which have been demonstrated to affect humoral and cell-mediated immune responses.

Hutcherson et al demonstrates oligonucleotide immunopotentiators having at least phosphorothioate bond which are capable of eliciting an immune response are well established in the art. Kuramoto et al teach an oligonucleotide, comprising: 5'-AACGTT-3', 8-40 nucleotides in length with a modified backbone and strong immunostimulatory activity of certain oligonucleotides maybe due to the potent palindromes as being well known in the art. Thus leading to predictable results, it would be obvious to use the cited immunostimulatory oligonucleotide comprising 5'-AACGTT-3', (as disclosed by Kuramoto et al) as an immunostimulatory oligonucleotide, with a phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate, wherein each internucleotide linkage has a phosphate backbone modification (as disclosed by Hutcherson et al). Thus, it remains obvious to combine them (Hutcherson et al and Kuramoto et al), in order to take advantage of using the features of oligonucleotides with at least one or additional inter-sugar linkages (i.e. phosphorothioate) such as enhancing the uptake into cells and enhancing stability and affinity of the oligonucleotide, which have been demonstrated to affect humoral and cell-mediated immune responses. KSR forcloes the argument that a specific teaching, suggestion, or motivation is required to support a finding a obviousness. See the recent Board Decision Ex parte Smith, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007 (citing KSR, 82 USPQ2d at 1396) available at (<http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>).

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Hutcherson et al demonstrates oligonucleotides having at least one phosphorothioate bond are immunopotentiators with the ability to enhance uptake into cells and enhance stability and affinity of an oligonucleotide which affect humoral and cell-mediated immune responses. Kuramoto et al teach strong immunostimulatory activity of certain oligonucleotides maybe due to the potent palindromes. Hutcherson et al and Kuramoto et al disclose the teachings aforementioned above and also are well known in the art. Therefore, the immunostimulatory oligonucleotide comprising: 5'-AACGTT-3' of Kuramoto et al is well within the capabilities for one of ordinary skill in the art to be obvious to modify the immunostimulatory oligonucleotide comprising 5'-AACGTT-3', 8-40 nucleotides in length (as disclosed by Kuramoto et al) wherein the backbone is modified by phosphate backbone modification, wherein the phosphate backbone is a phosphorothioate, wherein each internucleotide linkage has a phosphate backbone modification (as disclosed by Hutcherson et al). The KSR decision sets forth "if a technique has been used to improve one device, and a person of skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill". Thus, the requirements of obviousness under the KSR decision are met.

Hutcherson et al demonstrates oligonucleotide immunopotentiators having at least phosphorothioate bond which are capable of eliciting an immune response are well established in the art. Kuramoto et al teach an oligonucleotide, comprising: 5'-AACGTT-3', 8-40 nucleotides in length with a modified backbone and strong immunostimulatory activity of certain oligonucleotides maybe due to the potent palindromes as being well known in the art. Chen et al teach a modified oligonucleotide covalently linked sterol, wherein the sterol is used as delivery complex is well known in the art. Thus leading to predictable results, it would be obvious to use the cited immunostimulatory oligonucleotide comprising 5'-AACGTT-3', (as disclosed by Kuramoto et al) as an immunostimulatory oligonucleotide, and to modify the immunostimulatory oligonucleotide covalently linked to a nucleic acid delivery complex (disclosed by Hutcherson et al) by inclusion of a sterol (as disclosed by Chen et al). Thus, it remains obvious to combine them (Hutcherson et al, Kuramoto et al, and Chen et al), even without an express statement of motivation. KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board Decision *Ex parte Smith*, --USPQ2d--, slip

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op. at 20, (Bd. Pat. App. & Interf. June 25, 2007 (citing KSR, 82 USPQ2d at 1396) available at (<http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>).

One would have a reasonable expectation of success because the use of certain antisense oligonucleotides having at least one phosphorothioate bond enhances immune stimulation(as disclosed by Hutcherson et al) is well known in the art.

**8. Examiner's Response to Arguments regarding evidence (i.e. references and Declaration) provided by Applicant.**

It is stated that in response to applicant's arguments on 2/1/2010 that the Office has not addressed the prior references as well as a Declaration that demonstrate the unpredictability of phosphorothioate linkages and has failed to provide a proper factual or legal basis for improperly dismissing the evidence.

In regards to Applicants argument of the unpredictability of phosphorothioate linkages with support from references Stein et al and Perez et al cited by Applicant is not found persuasive. The reference (Stein et al ) cited by Applicant is not commensurate in scope with the claimed invention because Stein et al disclose the potential use of phosphorothioate oligos to enhance viral replication as inhibitors and the claimed invention is drawn to immunostimulatory oligonucleotides. The reference (Perez et al) cited by Applicant is not commensurate in scope with the claimed invention because although the particular oligonucleotide inhibited gene expression and one should use caution when considering oligonucleotides with phosphorothioate backbones because of the danger of nuclear transcription factor induction does not mean that all oligonucleotides including antisense oligonucleotides modified with a phosphorothioate backbone will be capable of inhibiting gene expression and have non-specific antisense effects.

Moreover, the Declaration of Dr. Cy Stein filed 3/12/2009 is insufficient to overcome the obviousness rejection for the reasons set forth in the previous Office action. Applicant refers to the Declaration of Dr. Cy Stein filed in an application separate from the instant application. Declarations, such as those submitted under 37 CFR 1.130, 1.131, and 1.132, filed during the prosecution of an application separate from the instant application do not automatically become a part of the instant application. Where it is desired to rely on an earlier filed declaration, the

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applicant should make the remarks of record in this application and include a copy of the original declaration filed in the prior application. Moreover, the declaration include(s) statements which amount to an affirmation that the affiant has never seen the claimed subject matter before.

Therefore the Declaration of Dr. Cy Stein is insufficient to overcome the rejection based upon it was a declaration made in the prosecution of another case and was not properly executed for use in the application. Therefore Dr. Cy Stein's statements regarding unpredictability of phosphorothioate backbones modification with immunostimulatory oligonucleotides are deemed unpersuasive.

**Therefore Applicants arguments on 2/1/2010 have been addressed by Examiner in regards to the issues related to the evidence (i.e. references and Declaration) cited by Applicant to rebut prima facie obviousness rejections.**

#### *Conclusion*

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m. If attempts to reach the examiner by telephone are unsuccessful, the acting examiner supervisor, Patricia Duffy can be reached on 571-272-0855. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. A. A./

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Nina A Archie

Examiner

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/N. M. Minnifield/

Primary Examiner, Art Unit 1645